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Questions as to the habitability of any area where soil is contaminated with TCDD are necessarily linked to considerations of excess risks of developing specific adverse health effects as a result of the total cumulative dose which an individual receives. In turn, this cumulative dose is a function of several factors:

(1) concentrations of environmental contamination

(2) location of and access to contaminated areas

(3) type of activities in contaminated areas

(4) duration of exposure

(5) specific exposure mechanisms

In addition, questions of continued habitability must also include considerations of the potential for limiting or eliminating ongoing exposures.

The development of a level of concern about an unacceptable risk due to exposure to TCDD is present poses significant difficulties because TCDD has such unique properties, as outlined in the preceding pages of this document.

As a first approach, a series of risk assessment estimates based on several of these factors has been utilized in the past by a number of groups in order to determine what an "acceptable" risk for exposure to TCDD would be. As more information on the toxicity of this chemical has become available, these levels have generally been reduced.

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In order to determine whether a specific concentration of TCDD in soil presents a risk to humans, it is first necessary to examine how humans might absorb TCDD from such soil. Unfortunately, it is not well-known how much of any chemical present in soil may be absorbed by humans coming in contact with such soil. Most risk assessments that have been made in the past have been made for such media as food where it is assumed that a certain amount of food with a certain concentration of the chemical in it is consumed, for air where it simply needs to be calculated how much air is inhaled, or for chemicals in water where the only number needed is the amount of water consumed, although, as far as water quality criteria are concerned, the bioaccumulation of chemicals in fish from contaminated water are also considered. Unfortunately, the analogous series of estimates is more complicated for soil.

There are basically three exposure routes that must be considered: dermal absorption through direct contact with the soil, ingestion of soil, and the inhalation of dust to which TCDD is attached. Vapors may be an additional, probably minor route of exposure. Another issue, which does not directly enter in the current risk assessment, is the fact that TCDD in the environment could eventually end up in the food chain particularly in fish. If TCDD enters a food chain, there is an unknown additional source of exposure which must be added to the risk of those individuals exposed to contaminated soil and of a larger, undefined population.

Regarding dermal absorption, there is some evidence that TCDD binds to the soil and would not be as easily available for absorption. (Vegetation covering contaminated soil may decrease TCDD availability as well.) However,

information on bioavailability is currently limited and may vary for different types of soil. According to the literature (Poiger and Schlatter, 1980, and a personal communication) anywhere from 1 to 10 percent of the TCDD which is in the soil may be absorbed through the skin, and this percentage is likely to be dependent on the TCDD concentration in the soil (i.e., it may be greater at higher concentrations) and on the type of soil. When Poiger and Schlatter (1980) applied soil with a dose of 350 ng TCDD to the backs of rats, 1.7 $\pm$ 0.5% of the dose was found in the liver; at a dose of 26 ng about 0.05% of the dose was found in the liver. It is not stated in the paper how long the soil was left in contact with the skin of the rats. Therefore, the subsequent estimates will take consideration of this range of skin absorption factors.

In regards to the portion of total dose due to ingestion of soil particles, feeding studies in animals suggest that 10-30% TCDD adsorbed on soil will be absorbed in the gastrointestinal tract. Poiger and Schlatter (1980) found 16-24% of the administered dose of TCDD in the liver. According to Fries and Marrow (1975) this represents about 70% of the body burden of TCDD. Therefore, the calculations to follow will also consider these differing gastrointestinal absorption rates.

In regards to inhaled doses, there is little information available on the amount of dust that may be present in the air in situations of known soil contamination; measurements in Seveso showed that the amount of dust in air was 0.14 mg/m^3 air (DiDomenico et al., 1980). No dust levels in air whose sole source is soil are available from air monitoring stations. Soil, vegetable matter and particles from other sources such as car exhaust are

measured as particulate matter. The use of particulate matter would highly overestimate dust derived from soil. It would be possible that in situations such as riding arenas or in relatively drier areas dust levels would be higher. On the other hand, immediately after a rainfall there would probably be less dust. In the same investigation, it was shown that TCDD levels in dust were comparable to those found in soil. Another unknown is the amount of material that could be carried into the house from the outside. In order to err on the conservative side, it is assumed that the exposure to dust inside a house surrounded by contaminated soil is similar to that which would occur if people spent their entire time in close contact with the contaminated soil outside. (One of the CDC sonsultants commented that the assumption that indoor levels will equal outdoor appear unnecessarily conservative.) It is further assumed that an average adult at rest exchanges approximately 10 m^3 of air per 24-hour period and that this would increase with mild activity to 18-24 m^3/day and to 40m^3/day with hard physical labor. Finally, it is assumed that whatever TCDD is inhaled adsorbed to dust particles is absorbed either through deposition in the respiratory tract or by ingestion after being brought up by the ciliary action of the respiratory tract epithelial cells.

For the sake of comparison, all of the above-discussed assumptions (and variations thereof) were applied in a series of total dose calculations. It was further assumed that individuals at risk are exposed to the maximum soil concentrations (e.g., 1 ppb and 100 ppb levels were used in the following calculations) continuously (i.e., total accessibility to contaminated areas).

Several comments were received from CDC consultants on exposure estimates. Unfortunately, there is no documentation in the literature which clarifies the problems raised. How much dirt does a young child eat when playing outside? How much dirt gets on the skin during gardening activities? How much dirt gets onto the skin of children playing football or other games? That information is simply not available. However, one gram of dirt less than 1mm thick can be spread over an area of 4-5cm^2 or 1 1/2 - 2 $inches^2$. Ten grams of soil less than 1 mm thick can be spread over an area of about 15 cm^2 or about 6 $inches^2$. (The volume of dirt will vary somewhat with moisture content.) The dirt used to give the above surface areas was Georgia clay which had been stored for several months at room temperature. The surface areas are illustrated in Figure 1. In Figure 2 surface areas of one palm of medium sized hands from adults and children were computed. These figures illustrate that it is not unreasonable that people will make contact with 1-10 grams of dirt. On a volume basis, 10 grams occupies 2 cm^3.

The estimates of contribution to total daily dose from percutaneous absorption given varying levels of TCDD concentrations in soil, quantities of soil on exposed skin surfaces and absorption rates are presented in Table 5. Table 6 contains the estimates of the daily dose derived from ingestion of varying amounts of soil contaminated at different levels with variable rates of gastrointestinal absorption. Finally, Table 7 represents the estimates of the contribution to total daily dose from inhalation of contaminated dust particles given the above assumptions.

All of the calculations regarding exposure are based on the assumption that humans have intimate contact with the contaminated soil and that a

percentage of the TCDD present in the soil is absorbed. The frequency of exposure must also be considered and for dermal exposure it must be remembered that clothing will afford some protection. The doses calculated in Table 5-7 are worst case estimates (e.g. amount of soil ingested is estimated for a child under 5 years of age) and the dose humans receive in most instances will be lower. If intimate contact was to less than 1 or 10 grams of soil or if the frequency of exposure and the % dermal absorption are somewhat reduced, the amount of absorbed TCDD would naturally also be less.

A large number of estimated total daily doses can be derived from the many combinations of the exposure route-specific doses (given different sets of assumptions as to absorption rates, soil contamination, etc.). For the sake of brevity, the two most extreme total daily dose estimates were compiled for 2 divergent levels of TCDD soil contamination (1ppb and 100ppb) and are as follows:

Lowest Daily Dose - 111.4 picograms/day for residential areas

Assumption: 1 ppb in soil; 1 gram of soil ingested (10% absorbed); 1 gram soil on skin (1% absorbed), daily exposure.

- 1.4 picogram/day for the general public in commercial areas.

Assumption: 1 ppb in soil; 1 gram of soil on skin (1% absorbed) once a week.

Highest Daily Dose - 400.14 nanograms/day for residential areas.

Assumption: 100 ppb in soil; 10 grams of soil ingested (30% absorbed); 10 grams soil on skin (10% absorbed).

- 140 picogram/day for commercial areas.

Assumption: 100 ppb in soil; 10 grams of soil on skin (10% absorbed) once a week

Of course, any other combination of these varying factors can be used to derive intermediate or farther outlying daily dose estimates. Appropriate adjustment for higher concentrations of TCDD in soil as for exposure to larger amounts of soil would have to be made.

Ingestion of soil would become negligible after age 5. Thus, daily doses after that age for soil containing 1 ppb would be 10 pg or 10000 pg about 140 fg/kg for adults weighing 70 kg, 200 fg/kg for adults weighing 50 kg and 300 fg/kg for children weighing 30 kg.

Risk Assessment

The critical step in assessing individual risks at these estimated dose levels must incorporate a comparison to known (or estimated) "safe" levels of exposure in relation to clearly defined health effects end-points.

The National Research Council of Canada (NRCC) has recently published a report reviewing available toxicity data for TCDD and related compounds as well as various procedures to calculate a "virtually safe dose" (VSD) for TCDD from such data. A summary table from this document listing the various models, estimated VSDs, approximate 95% confidence levels and references to the different models which were used was reviewed by the CDC consultants. It was

determined that the table contained a number of errors and the virtually safe dose was therefore recalculated as outlined in this section (Crump and Watson, 1979). The analyses in this section follow guidelines recommended by the CDC consultants and are based upon two studies: one by Kociba et al (1978) and another by the National Toxicology Program (NTP, 1981). Further detail on these (and other) studies can be obtained from the EPA TCDD risk assessment (EPA #: EPA-600/6-81-003). All of the CDC consultants agreed that the available human data are inadequate to be used in risk assessment calculations.

In the Kociba study a substantial proprotion of the animals including those in the control group died before the two-year sacrifice (78% to 92% in the males and 68% to 92% in the females). In addition, there appear to be time-related as well as dose-related effects at the lesion sites. No time-adjusted analysis of this data was done for this document; this may be accomplished by C. Portier of NIEHS if the individual animal data can be obtained.

The important lesion sites (for risk assessment) in the two sexes are given in Table 10 along with the tumor incidence at each dose. The original pathology done by Kociba was reviewed by Squire and the results of Squire's review are therefore also included. In the risk assessment done by the EPA, the analysis is based upon grouping these sites using as incidence the number of animals with any one of the lesions divided by the number of animals examined at any of these sites for each sex. We have not used this procedure; instead the multistage model was fit to the tumor incidence from each lesion site. These results appear in Table 9 along with the chi-squared value for the goodness-of-fit test. When the best fit to the data was non-linear, the linear

model was also fit (see the note at the bottom of Table 9 for a description of this model) and produced risk estimates for comparison. In all sites, except female liver tumors, it was possible to adequately fit the data. For males, the smallest lower confidence bound on the "virtually safe dose" (VSD) for an added risk of 1/1,000,000 is 117 femtograms/kg b.w./day. In females, the most sensitive site seemed to be the liver, but it was not possible to get an adequate fit using the administered dose. In the original manuscript, Kociba et al (1978) had determined the concentration of TCDD in the livers of a sample of the sacrificed animals from each dose group. The means for each dose group appear below:

Administered dose:	0.001	0.01	0.1
Liver dose (ppb)	0.540	5.10	24.0

Assuming these concentrations were present in the animals at stable levels for much of the study, these are the appropriate doses to which the liver tumor incidence data should be fit. Assuming the relationship between administered dose and liver dose is non-linear above the 0.01 ug/kg b.w./day dose and linear below this does (as appears to be the case), liver dose can be transformed back to administered dose using the least-squares line through the points (0,0), (0.001,0.54) and (0.01,5.1). This leads to the linear relationship;

Administered dose = Liver dose/510.297.

The VSD estimates and lower confidence bounds in the administered dose scale appear in Table 9 under model type "TRANSF". Using this approach, the smallest

lower confidence bound on the VSD using an added risk of 1/1,000,000 cancers is 27.6 femtograms/kg b.w./day for female rats.

The NCI/NTP study (1981) was a gavage experiment on B6C3f1 mice and Osborne Mendel rats, both sexes. There were 75 vehicle treated control animals and 50 animals at each of three doses for each sex by species combination. The doses were administered twice weekly. In order to use the same scale, these weekly doses were divided by seven obtaining daily doses. There are of course questions of peaks and dips in body content of TCDD. We have assumed that in a weekly scale the dose is approximately constant, and division by 7 to yield daily doses is an acceptable conversion. Both sexes in rats and male mice received doses of 0.0014, 0.0071 and 0.0714 ug/kg b.w./day (0.01, 0.05 and 0.50 on the weekly dose scale). Female mice received doses of 0.0057, 0.0286 and 0.2859 ug/kg b.w./day (0.04, 0.2 and 2.0 on the weekly scale). There were no significant survival differences in any group and in fact the estimates of the VSD based upon a time-to-tumor model (multistage Weibull) were similar to the estimates obtained from the linear model.

The important lesion sites, the estimates of risk and the chi-squared goodness-of-fit statistic are given in Table 10. As before, when the linear model was not the best fit, it was fit separately in order to see what difference this model would make. All of the models gave acceptable fits to the data. Where there are two or more lesion sites for a particular animal group, the EPA pooled the results as mentioned before. Again, combining of independent sites was not done here.

The smallest lower confidence bounds on the VSD (1.E-6) for each sex/species combination are as follows: male rat thyroid 214; female rat liver nodules and carcinomas 160; male mouse liver adenomas and carcinomas 86; and female mouse lymphoma/leukemia 543. These results do not differ markedly from the results of the Kociba study.

Thus, the risk assessment calculations for the different tumors in these 2 studies provide a dose range of 280 femtograms/kg b.w./day to 14.3 picograms/kg b.w./day that would result in an increased cancer risk of one per 100,000 , and a dose range of 28 femtograms/kg b.w./day to 1428 femtograms/kg b.w./day that would result in an increased cancer risk of one per 1,000,000. In making the above predictions direct conversions were used from rodents to men. It is presently not clear whether this is justified. Humans are better able to repair DNA than rodents, and many other differences could be pointed out. However, there is no scientifically justified alternative form of extrapolation (e.g. use of safety factors) which could be used.

These calculations assume that a linear dose response relationship exists for carcinogens which are primarily promoters. This, however, has not been shown experimentally and it is presently not understood how promoters affect cancer growth at very low concentrations. TCDD apparently affects cell membranes through lipid peroxidation (Stohs et al. 1983) which also affects membrane fluidity. Lipid peroxidation most likely is the reason for the formation of multinucleated cells in TCDD exposed animals (Jones and Butler, 1974). It is not clear whether at very low dosage levels antioxidants such as Vitamin E, Vitamin C, Selenium and unsaturated fatty acids would have a

protective effect against the promoting actions of TCDD. It has also been established that TCDD increases the absorption of iron which results in increased liver toxicity (Sweeney et al. 1979). For these reasons and the receptor model developed by Poland it is not known whether the linear derived multi-stage model for the cancer risk assessment is the most appropriate. Unfortunately a scientific data base which would permit the use of different, possibly less conservative models, presently does not exist.

Since the no observable effect levels for reproduction, immune toxicity and various other toxic effects are not established in various species, a conservative approach for chronic toxicity in general is in order. The study by Murray et al. (1979) suggested that 0.00lug/kg/day is a no observed effect level for reproduction in rats. Nesbit and Paxton (1982) recalculated the data developed by Murray et al. (1979), by using results from different generations as independent variables which is a somewhat unorthodox procedure. They concluded that 0.001 ug/kg b.w./day was still an effect level. However, this study shows a very varied fertility index among the controls through different generations; in addition, TCDD body burdens of the dams are greatly affected by lactation introducing another variable. Drs. Hoel, Van Ryzin and Portier among the CDC consultants also reviewed these data and concluded that there was insufficient evidence for an effect at .01 ug/kg b.w./day. For these reasons this study is not used for risk assessment calculations (see also Appendix II).

Subhuman primates (which are much more susceptible to the effects of TCDD) show an effect on reproduction if fed for six months at a daily dose of 1.8 ng/kg. If the toxicology data from subhuman primates is used, then a 1000-fold

safety factor would have to be used, since the lowest dose of 1.8 ng/kg per day was not a no-observed effect level and was not obtained from a chronic feeding study. Thus a daily dose rate of 0.0018 ng/kg--corresponding to a total daily dose of 144 picograms--would be tolerable for an 80 kg person. For a 60 kg person this would be 108 pg. Thus at the lowest daily dose likely to obtain as estimated above for a soil level of 1 ppb (111.4 pg/day), both of these extrapolations from reproductive studies in animals appear to suggest a situation of no excess risk in humans. However, at virtually all other estimated levels of daily dose (i.e., under more severe sets of assumptions or the higher level of TCDD in soil) one might expect the induction of adverse reproductive health effects.

Taking the most sensitive cancer risk estimate of 28 femtograms/kg b.w./day for an increased lifetime risk of 1×10^{-6}, this is less than the amount of TCDD conceivably absorbed from soil contaminated with TCDD at 1 ppb, even using the lowest estimates for calculating absorbed dose. However, it must be stressed that the exposure assessments used in estimating risks for carcinogenicity and reproductive health effects contain critical assumptions which are not likely to be obtained in reality. Most prominent of these are the assumptions of uniform levels of contamination throughout the living space and constant, total access to these areas. In fact, the situation is likely to be such that areas with elevated TCDD levels, which, of themselves, can be expected to decrease over time, are found in specific, well-defined locations which have concomitant unique use and access characteristics. Therefore, in such a situation where access is less than total and constant, the actual daily exposure will be lower. Similarly, different usage patterns of affected areas

(e.g., sports activities, gardening, horseback riding) or an individual's characteristics (e.g., pica in children) are not likely to lead consistently to worst case situations and will have differing effects on the determination of total cumulative dose. Similarly, soil ingestion for adults is not likely to approach that for children, the worst-case group. Even if all of these assumptions were to be accepted as being valid at all times, at the lowest daily dose levels estimated above for soil TCDD contamination of 1 ppb (i.e. 111.4 pg/day) it would take almost several years to accumulate a total dose sufficient to increase an individual's risk of developing cancer by one in a million. We have therefore concluded that soil levels of 1 ppb TCDD in residential areas is a reasonable level to express concern about health risks.

Implications for Risk Management

Therefore, where residential soil levels exceed 1 ppb, risk management decisions on habitability and limiting exposure may range from recommendations to avoid identified "hot spots" or limit specific activities in these areas (if possible) or temporary relocation while clean-up and/or onsite stabilization of the contaminations are performed to permanent relocation and access restriction for a given site. In addition, such recommendations will have to be prepared in terms of situations which range from the need for near-term action to those of a less emergent nature. In all of these scenarios, however, these decisions must be made on a site-specific basis as indicated by the complexities and variability of circumstances discussed in the body of this document.

Although from these calculations levels of TCDD below 1 ppb are, for practical purposes, considered not to reach a level of concern, a number of

additional considerations related to the risk assessment calculations should be pointed out to decision makers involved in risk management:.

1. The calculations for this level take into consideration that exposure most likely will not be consistent for a lifetime, since TCDD will slowly degrade, nor will people be exposed extensively to the soil on a continuous daily basis. For instance, it is anticipated that during cold weather, and while it is raining, not much outside activity will occur. From the limited available information it appears also that levels of TCDD within houses are at least 100-fold less than what is measured outside the houses.
2. It is presently not known what the precise bioavailability of TCDD from soil is.
3. The recovery of TCDD from soil that is extracted for chemical analysis varies a great deal and may be as low as 20%.
4. It has been shown by Fries et al. (1982) that cattle, sheep, and swine consume up to 7% soil/day of their total ingested dry matter when grazing on ranges. From experience with polybrominated biphenyls and 1,2,3,6,7,8-hexachlorodibenzodioxin, it seems that levels in adipose tissue of these animals will bioaccumulate (see risk assessment scenario for ranges). Soil levels of TCDD on ranges and other farmland should, therefore, not be any higher than the levels given in Table 12.
5. Furthermore, if contaminated soil is close to waterways and can contaminate these waterways by way of erosion, levels may also have to be lower, since fish can bioconcentrate TCDD 20,000-fold (NRCC, 1981) or more. Action levels for fish have been set by the FDA; at

50 ng TCDD/kg edible portion, fish should not be consumed, and at 25-50 ng/kg, fish should not be consumed daily.